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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/696,530	10/24/2000	Lars Wahlberg	19313-004 (NS-4)	4889
35437	7590	03/17/2004	EXAMINER	
MINTZ LEVIN COHN FERRIS GLOVSKY & POPEO			NICHOLS, CHRISTOPHER J	
666 THIRD AVENUE			ART UNIT	
NEW YORK, NY 10017			PAPER NUMBER	

1647

DATE MAILED: 03/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/696,530

Applicant(s)

WAHLBERG ET AL.

Examiner

Christopher J Nichols, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,3,5-15,17-22 and 42-56 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 7, 22, 42, 43, and 50 is/are rejected.
- 7) ☒ Claim(s) 5,6,8-15,17-21,44-49 and 51-56 is/are objected to.
- 8) ☒ Claim(s) 1,3,5-15,17-22 and 42-56 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 April 2003 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. The Response and Amendment filed 5 January 2004 has been received and entered in full. In view of Applicant's amendments and explanation of neuronal markers DXL1, MEIS2, and PAX6 finality of the previous Office Action is hereby *withdrawn* and prosecution on the merits reopened.

Specification

2. The disclosure is objected to because of the following informalities:

pp. 9 line 9 "such as ," (unnecessary space)

pp. 9 lines 15-16 "Meis2" replace with "MEIS2" (gene names generally capitalized)

pp. 9 lines 9-10 "beta-III-tubulin" replace with "beta-tubulin III"

pp. 9 line 10 "recognizing ,beta-tubulin" replace with "recognizing, beta-tubulin"

pp. 14 line 1 "(e.g., , β -tubulin III)" (unnecessary space)

pp. 14 line 16 "(TGF,s,)" replace with "(TGFs)"

pp. 15 line 8 "dopamine-,hydroxylase" (space?)

pp. 18 line 24 handwritten correction? Replace with " α -galactosidase"

pp. 20 line 28 "2x HeBS" replace with "2X HBS"

pp. 21 line 16 "TGF,s," replace with "TGF"

pp. 25 line 2 "acid, TNF \cdot , MIP-1 \cdot , MIP-1,, MIP-2" replace with "acid, TNF, MIP-1, MIP-2"

pp. 26 line 4 "TGF,,," replace with "TGF,"

pp. 28 line 23 "and ,beta-tubulin III" replace with "and beta-tubulin III"

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pp. 28 line 25 “the ,beta-tubulin III” replace with “the beta-tubulin III”

pp. 28 line 28 “Meis2” replace with “MEIS2” (gene names generally capitalized)

pp. 29 line 16 “and ,beta-tubulin III” replace with “and, beta-tubulin III”

pp. 31 line 8 “marker ,beta-tubulin III” replace with “marker, beta-tubulin III”

pp. 31 line 25 “CO₂” replace with “CO₂”

pp. 33 line 22 “GFAP⁰” replace with “GFAP⁺”

pp. 33 line 27 “occasionally ,beta-tubulin III⁺” replace with “occasionally, beta-tubulin III⁺”

pp. 35 line 10 “beta-III-tubulin” replace with “beta-tubulin III”

pp. 35 line 11 “beta-II-tubulin” replace with “beta-tubulin III”

pp. 35 line 24 “marker ,beta-tubulin III” replace with “marker, beta-tubulin III”

pp. 35 line 25 “Meis2” replace with “MEIS2” (gene names generally capitalized)

pp. 36 line 2 “also ,beta-tubulin III⁺” replace with “also, beta-tubulin III⁺”

pp. 37 line 12 “Example 4)were” replace with “Example 4) were”

pp. 37 line 14 “cells/OI” replace with “cells/pl”

3. Appropriate correction is required.

Claim Objections

4. Claim 3 is objected to because of the following informalities: the inclusion of “(i.e., nestin⁺)” is not necessary. The notation of “nestin⁺” to denote that a cell is nestin immunoreactive is well accepted in the art. The inclusion of material in parentheses is prone to confusion.

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5. Claims **47** and **54** are objected to because of the following informalities: both contain spelling mistakes.
6. Claims **53** and **54** are objected to because of the following informalities:
 - a. claim 53 recites "...cells are immunoreactive with cortical neuronal markers" this is inconsistent with the Specification and claim 46 which states "cells are not immunoreactive with cortical neuronal markers". Examiner requests clarification if this is the actual limitation or an inadvertent typo dropping "not" from claim 53.
 - b. claim 54 recites "...wherein the cortical neuronal markers is PAX3" this is inconsistent with the Specification and claim 47 which states "...wherein the cortical neuronal markers is PAX6". Examiner requests clarification if this is the actual limitation or an inadvertent typo in claim 54.
7. Appropriate correction is required.
8. Claims **5**, **6**, **8-15**, **17-21**, **44-49**, and **51-56** are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

112 Rejection

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claim **22** is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant

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regards as the invention. Steps (c) and (d) of claim 22 are not steps *per se* but statements of desired cell properties.

10. Claim 48 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. A word is missing in the first line of the claim.

11. Claims 7, 43, and 50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “GABA-ergic phenotype” is indefinite. It is not clear whether expressing GABA_A or GABA_B receptors; GAD₆₅ or GAD₆₇, GABA transaminase, or GABA transporter defines what the Applicant considers a “GABA-ergic phenotype”.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

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12. Claim **42** is rejected under 35 U.S.C. 102(b) as being anticipated by Miyaguchi (October 1997) "Ultrastructure of Intermediate Filaments of Nestin- and Vimentin-Immunoreactive Astrocytes in Organotypic Slice Cultures of Hippocampus." Journal of Structural Biology **120**(1): 61-68. Miyaguchi (1997) teaches isolated cultures of nestin⁺ and GFAP⁺ positive astrocytes, which are not tumorigenic thus meeting the limitations of claim 42 (Figure 1).

13. Claim **42** is rejected under 35 U.S.C. 102(b) as being anticipated by Hulspas *et al.* (November 1997) "*In Vitro* Cell Density-Dependent Clonal Growth of EGF-Responsive Murine Neural Progenitor Cells under Serum-Free Conditions." Experimental Neurology **148**(1): 147-156. Hulspas *et al.* teaches isolated cultures of murine cells which are both nestin⁺ and GFAP⁺ positive and not tumorigenic thus meeting the limitations of claim 42 (pp. 151).

14. Claim **42** is rejected under 35 U.S.C. 102(b) as being anticipated by Schinstine & Iacovitti (September 1996) "Expression of Neuronal Antigens by Astrocytes Derived from EGF-Generated Neuroprogenitor Cells." Experimental Neurology **141**(1): 67-78. Schinstine & Iacovitti teach isolated cultures of murine astrocytes which are both nestin⁺ and GFAP⁺ positive and not tumorigenic thus meeting the limitations of claim 42 (Figure 1).

15. Claims **1**, **3**, and **22** are rejected under 35 U.S.C. 102(e) as being anticipated by US 6,294,383 B1 (25 September 2001) Isacson & Dinsmore.

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16. Claims 1 and 3 are drawn to cell cultures which are 90% GFAP+, capable of differentiating into neurons, divide in the presence of EGF, amphiregulin, aFGF, bFGF, TGF α , or a combination thereof, differentiate in serum free and growth factor free conditions wherein greater than 50% of the cells are nestin⁺ under proliferation-promoting culture conditions. The Specification teaches that the cells were obtained from the lateral ganglionic eminence (Examples 1 and 2).

US 6,294,383 teaches a population consisting essentially of isolated fetal porcine lateral ganglionic eminence cells obtained from an embryonic pig of gestational age of between about 20 to about 50 days (Claim 1). Since it has been established by the courts that a product inherently possesses characteristics of that product (i.e. including the amino acid sequence of a protein). See, e.g., *Ex parte Gray*, 10 USPQ 2d; *In re Best*, 195 USPQ 430). In addition,

“the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved”. *Ex parte Gray*, 10 USPQ 2d 1922 (1989); *In re Best*, 195 USPQ 430 (CCPA 1976).

Moreover, when the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe.*, 227 USPQ 964, 966 (Fed. Cir. 1985); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). Lastly it is noted that the courts have held that when the prior art product reasonable appears to be the same as that claimed, but differs by process in which it is produced, a rejection of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a

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patentable difference (*In re Brown*, 173 USPQ 685). Thus since the cells of claims 1 and 3 are obtained from the same embryonic structure as the cell population of US 6,294,383 the cells are taken to share the same properties absent evidence to the contrary-.

17. Claim 22 is drawn to a method of isolating the cell cultures as described above. The Examiner notes that steps (c) and (d) are not steps *per se* but statements of cell properties. Thus US 6,294,383 anticipates claim 22 because it teaches obtaining a cell population through a method comprises dissecting out the lateral ganglionic eminence from a fetal pig, dissociating said cells in culture thus meeting the limitations of steps (a) and (b) of claim 22 (Col. 24-25).

Summary

18. No claims are allowed.

19. The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon are considered pertinent to the instant application:

- c. US 6,258,353 (10 July 2001) Isacson & Dinsmore

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on **(571) 272-0887**.

The fax number for the organization where this application or proceeding is assigned is **703-872-9306**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

CJN
March 16, 2004


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